

Please charge the fee of \$54 for the three extra claims of any type added herewith, to Deposit Account 25-0120.

REMARKS

The claims are amended herewith in a manner that overcomes the indefiniteness rejection, and is believed to place the application in condition for allowance at the time of the next Official Action.

At pages 2-3 of the Official Action, claims 8, 9, 12, 14, 16 and 17, as previously in the case, were rejected for indefiniteness.

It is believed to be apparent that the amendments made to those claims herewith are effective to overcome that rejection. Applicants acknowledge with appreciation the Examiner's helpful suggestions for overcoming certain of the informalities in the claims as originally filed. As to claims 14, 16 and 17, which recited preferred aspects within general aspects, the preferred aspects are deleted from those claims and made the subject of new claims 23-25.

It is therefore believed that the rejection of certain of the original claims for indefiniteness should be withdrawn and not repeated with respect to any of the claims as they now appear in the case.

Claims 1-22 were rejected under 35 USC §103(a) as allegedly being obvious over GARDINER 6,136,339 in view of WEINSTEIN et al. 6,013,290, WO 96/04240, FANG 5,886,040,

Webster's Dictionary (10th Edition), ODIAN et al. (Schaum's Outline), HULTMAN et al. 5,767,159 and ST. CYR et al. 6,159,942.

That rejection is respectfully traversed, for the following reasons.

The ensuing discussion will address wherein the proposed combination of eight references, applied in relation to a composition which, in its simplest form, comprises only three ingredients, fails to render *prima facie* obvious the subject matter of any present claims 1-25. Moreover, the ensuing discussion will highlight aspects of the disclosure provided in the specification which serve to rebut and forestall any *prima facie* case of obviousness which might otherwise be made out by the applied combination of references.

The Proposed Combination of Eight References does not Render Prima Facie Obvious any of Present Claims 1-25

The eight references sought to be applied in combination contain no explicit or implicit suggestion or motivation that their disclosures ought to be combined selectively in any manner that would be necessary to produce the claimed invention. On the contrary, it is believed to be apparent that, only with the benefit of hindsight might the claimed invention be reconstructed from the teachings of the applied references. Applicants therefore respectfully traverse the proposed obviousness rejection, on the basis that the skilled artisan at the time the invention was made, and absent

foreknowledge of the invention, would not have had the requisite motivation to arrive at the claimed invention from their collective teachings.

Furthermore, applicants respectfully disagree with the Examiner's opinion that based on the combination of two or more of the eight references the skilled artisan would arrive at the claimed invention. The cited references fail to provide any teaching, alone or in combination, that would have suggested the combination of creatine, at least 75% of the daily recommended value of phosphorus and a blood buffer.

Thus, absent the present disclosure, a composition containing creatine, at least 75% of the daily recommended intake of phosphorus (i.e. more than about 500 mg, especially more than about 1 g per day), and a blood buffer would not have been obvious to one skilled in the art from the reading of the cited references.

The cited references do not teach a combination of creatine, phosphorus and blood buffer, not do the cited references relate to the problems or improvements relating to combinations of creatine and relatively high amounts of phosphorus per serving, nor do the cited references alone or in combination suggest that blood buffer possesses the capability to counteract the adverse effects of administration of creatine and at least 75% of the daily recommended intake of phosphorus. The skilled artisan would thus not conclude from the cited reference

that a combination of creatine, at least 75% of the daily recommended intake of phosphorus and blood buffer has advantageous effects.

Applicants also wish to point out that none of the cited references recognize the problem which has been solved by the inventors and that none of the cited references nor any combination gives any hint as to the applicants' invention.

GARDINER is cited as disclosing a food supplement comprising creatine, including creatine monohydrate, creatine citrate and creatine pyruvate and phosphorus and salts thereof.

The food supplement described by GARDINER contains lipoic acid and creatine. GARDINER believes that insulin is a primary factor that stimulates creatine transport into the muscle cells, and that lipoic acid both mimics and enhances the actions of insulin (column 2, lines 7-9). GARDINER thus points to the creatine transport as being insufficient and a main target for improvement of body performance. Based on GARDINER, the skilled artisan would thus look to further improve creatine uptake in order to improve body performance. Based on the disclosure of GARDINER, the skilled artisan would thus not seek solutions for improving body performance by counteracting adverse effects, and therefore would not have arrived at the present invention. GARDINER thus points in a different direction as to improvements of body performance, compared to applicants' invention. The

skilled artisan would thus not have arrived at the invention having read GARDINER's disclosure.

Furthermore, GARDINER describes exemplary creatine preparations, which may be used in the food supplement and additionally gives a list of minerals, which may be used in the food supplement. GARDINER, however, does not give any indications as to a preferred combination of a creatine preparation and a mineral selected from the two lists, and thus does not teach the combination of creatine, phosphorus and blood buffer. A skilled artisan would thus have to select components from two different lists of components to arrive at the combination of creatine, phosphorus and blood buffer, and GARDINER does not give any hint as to such selection. Thus, a combination of creatine, phosphorus and blood buffer therefore cannot be regarded as obvious over GARDINER.

Additionally, GARDINER does not teach the advantageous inclusion of at least 75% of the daily recommended intake of phosphorus in a product. GARDINER discloses that the composition may include minerals in conventional amounts, for example ranging from 0.01 mg to about 100 mg per gram of food serving (column 3, lines 35-39). It would be unclear to the skilled artisan which amounts of which mineral should be included in the composition since a) the amounts refers to a single mineral or mixtures of minerals or salts thereof and b) the mineral may be administered in an amount ranging from 0.01 mg to about 100 mg per gram of

food serving. Since a food serving can weigh 10 to 500 g (column 4, line 16), the minerals may be administered in an amount ranging from 0.1 mg to 50 g mineral per food serving. The skilled artisan would not have been able to conclude any sensible suggestion as to what amounts of a particular mineral to include in the food supplement, and thus would have consulted the examples as to what amounts of minerals or mixtures thereof are suitable. In the examples, GARDINER teaches that a serving contains 100 mg or 50 mg phosphorus, which is equivalent to 10% and 5% of the daily recommended intake of phosphorus. GARDINER thus does not provide any hint at the advantageous inclusion of at least 75% of the daily recommended value of phosphorus in a serving.

In conclusion, GARDINER does not teach a combination of creatine, phosphorus and blood buffer, nor does the reference provide any teaching that suggest the inclusion of blood buffer in a serving which includes at least 75% of the daily recommended intake of phosphorus and creatine. GARDINER's disclosure even points the skilled artisan in a different direction for improving body performance (increase of creatine transport) compared to applicants' invention (reducing adverse effects of increased glycolysis). Therefore, one skilled in the art would not have arrived at applicants' invention of compositions containing creatine and at least 75% of the daily recommended intake of phosphorus per serving and blood buffer, having looked at

GARDINER, nor would GARDINER in combination with one or more of the cited references make applicants' invention obvious.

WEINSTEIN et al. 6,013,290 is cited as disclosing that for persons who are exercising and replenishing lost water, sodium is necessary to prevent hyponatremia and allows optimal restoration of lost fluid. WEINSTEIN et al. is also cited to disclose that carbohydrates are useful for recovery of muscle glycogen after exercising; that sodium bicarbonate, sodium citrate and potassium citrate are alkaline buffers improving performance in athletes utilizing the anaerobic energy system by counteracting the increasing acidity caused by exercise and which acidity contributes to fatigue; creatine supplementation for allows higher rates of ATP resynthesis; and that phosphates and pyruvates may have positive effects on exercise.

The main goals of the nutrient beverage formulations as provided by WEINSTEIN et al. are to prevent fluid loss by ingestion of fluids, maintain appropriate levels of electrolytes and increase carbohydrates in the body prior to exercise (column 2, lines 34-42). WEINSTEIN et al. also discloses that other agents are optionally included in the formations and optional agents, which may or may not have positive effects. The skilled artisan might learn from this disclosure that appropriate levels of water in the body are important for body performance. However, the skilled artisan would not be able to make any sensible selection from the list of optional agents, since

WEINSTEIN et al. does not provide any directions as to a proper selection, for example because WEINSTEIN et al. explicitly mentions that optional components such as phosphates, may or may not have positive effects. Because of this lack of clarity with respect to the effectiveness of the optional components, the skilled artisan would therefore not have been motivated to include relatively high amounts of phosphorus in a composition, since it may not have a positive effect. Applicants thus respectfully disagree that the skilled artisan would arrive at applicants' invention based on WEINSTEIN et al. alone or in combination with one or more of the cited references.

Additionally, WEINSTEIN et al. did not recognize nor mention the advantageous inclusion of at least 75% of the daily recommended value of phosphorus in a supplement for improvement of body performance. The skilled artisan would thus not look at this document when faced with the task of improving compositions for enhancing body performance containing creatine and at least 75% of the daily recommended value of phosphorus.

Furthermore, since WEINSTEIN et al. has not recognized any adverse effects of inclusion of creatine and relatively high amounts of phosphorus, the skilled artisan would not conclude from WEINSTEIN et al. or any of the cited references together with WEINSTEIN et al. that compositions containing creatine and at least 75% of the daily recommended value of phosphorus can be further improved by combining creatine and at least 75 wt.% of

the daily recommended value of phosphorus per serving with blood buffer.

In conclusion, this disclosure fails to provide any hint towards the invention as claimed herein.

In retrospect, it may be possible to find in GARDINER and WEINSTEIN et al. the elements of the present invention. However, a proper obviousness assessment requires an analysis starting from the prior art without knowledge of the invention. Such an analysis does not demonstrate a motivation to combine the elements of the invention, and to arrive at the benefits thereof.

NEGRISOLI et al. (WO 96/04240) relates to hydrosoluble creatine in water and methods for the preparation of hydrosoluble creatine salts. The document does not teach a composition comprising creatine and phosphorus. The document thus does not give the skilled artisan any hint as to improvements relating to the combination of creatine and relatively high amounts of phosphorus. Applicants respectfully disagree that NEGRISOLI et al. can provide any basis for non-obvious objections, alone or in combination with other documents.

FANG relates to creatine pyruvate. Creatine pyruvate is described in the document as a solution towards the limited palatability of pyruvate and creatine alone. FANG does not teach any combination of creatine and phosphorus, a combination of creatine and blood buffer, or a combination of phosphorus and blood buffer. Additionally, FANG does not teach a combination of

creatine, phosphorus and blood buffer, not does FANG provide any teaching as to the advantageous inclusion of blood buffer in a composition comprising a combination of creatine and at least 75% of the daily recommended intake of phosphorus.

Furthermore, FANG relates to the problem of reduced palatability of compositions containing creatine and pyruvate. The skilled artisan would thus not consult this document when attempting to improve body performance via food supplements containing creatine, however, may use this document in an attempt to improve the palatability of compositions containing creatine and pyruvate.

FANG thus cannot provide any basis for obviousness objections, alone or in combination with other documents.

Webster Dictionary (10th Edition) is cited as disclosing the definition of "precursor". Applicants believe this disclosure provides no support to the rejection of the present claims.

ODIAN et al. describe the Krebs cycle. ODIAN et al. however does not relate to improvements of body performance nor does it relate to compositions containing creatine, phosphorus and blood buffer. Therefore, this document likewise lacks relevance to the present invention.

HULTMAN et al. relates to a method for increasing the muscle performance capability in mammals by administering to the mammal at least 15 grams of creatine. HULTMAN et al. explains

his view on the intracellular function of creatine phosphate (column 1, lines 22-30). This does thus not in any manner relate to oral administration of creatine phosphate. In fact, HULTMAN et al. teaches that phosphocreatine can hardly be used in a therapeutic situation, as it cannot pass the cell membrane (column 2, lines 48-49). Additionally, HULTMAN et al. does not teach that the administration of phosphorus with creatine provides advantageous effects. The lack of a recommendation to advantageously combine phosphorus and creatine and the recommendation to exclude phosphocreatine from a preparation for improvement of body performance even teaches away from the combination of creatine and at least 75% of the daily recommended value of phosphorus and thus does not in any manner relate to a combination of creatine, at least 75% of the daily recommended value of phosphorus per serving and blood buffer.

In conclusion, this disclosure fails to provide any hint towards the claimed invention.

ST. CYR et al. describes methods for increasing the energy levels of healthy humans by orally administering an effective amount of a pentose to said human, optionally combined with creatine. The document does not provide a combination of creatine and phosphorus, creatine and blood buffer or blood buffer and phosphorus, nor does it suggest to combine a blood buffer in a composition comprising a combination of creatine and

at least 75% of the daily recommended intake of phosphorus and creatine.

Thus, it is believed that this document, alone or in combination, cannot provide a basis for an obviousness rejection.

The Present Specification Contains Evidence of Unexpected Results Effective to Rebut and Forestall any Prima Facie Case of Obviousness Based upon the Eight Applied References

As disclosed by applicants, power output can be improved using creatine and/or phosphorus. Creatine provides an improvement in power output of 3%, administration of phosphorus improves the power output by 3% and the combination of creatine and phosphorus and creatine improves the power output by 6% (applicants' disclosure, page 10, Table 1). Applicants found that administration of creatine and blood buffer improved anaerobic working capacity 15.6% and that co-administration of creatine, at least 75% of the daily recommended dosage of phosphorus per serving and blood buffer markedly improved the anaerobic working capacity with 49.8% (see applicants' disclosure, page 18, Table 2), which is the result of a surprisingly synergistic and unexpected effect (see applicants' disclosure, page 8, line 4).

These tests, both inside and outside the range of the invention, show the criticality of the inclusion of blood buffer in a composition containing creatine and at least 75% of the daily recommended value of phosphorus per serving. The unexpected and synergist results of applicants' invention is thus

sufficiently established. The presence of these results that are greater than expected are evidence of non-obviousness (MPEP 716.02).

As the Examiner is aware, when the specification itself contains evidence of unexpected results, this must be accorded the same weight as a Rule 132 declaration, and must be considered in the first instance in assessing whether the prior art makes out a *prima facie* case of obviousness. As held, for example, by the U.S. Court of Appeals for the Federal Circuit in the case of *In re Wright*, 6 USPQ2d 1959 (Fed. Cir. 1988),

Factors including unexpected results, new features, solution of a different problem, novel properties, are all considerations in the determination of obviousness in terms of 35 USC §103. When such factors are described in the specification they are weighed in determining, in the first instance, whether the prior art presents a *prima facie* case of obviousness. Emphasis added, 6 USPQ2d at 1962.

Additionally, it is respectfully pointed out that based on the above cited references, the skilled artisan would not conclude that ingestion of creatine, at least 75% of the daily recommended value of phosphorus per serving and blood buffer would provide an improvement in anaerobic working capacity of about 50%. In fact, the references cited are silent on improvements of anaerobic working capacity (AWC) with combinations of creatine, phosphorus and blood buffer.

The absence of any hint towards the improvement of AWC with a combination of creatine, at least 75% of the daily recommended value of phosphorus per serving and blood buffer and

the marked synergistic improvement of AWC due to the ingestion of the novel composition according to applicants' invention thus overcomes the *prima facie* obviousness rejection.

From the above discussion, therefore, it is believed to be apparent that the proposed combination of eight references cannot be considered to render *prima facie* obvious the subject matter of any of present claims 1-25, particularly in view of the showing of unexpected results provided by the present specification.

Favorable reconsideration and withdrawal of the prior art rejection are therefore respectfully requested.

In view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now in condition for allowance, with claims 1-25, as amended. Allowance and passage to issue on that basis are accordingly respectfully requested.

Attached hereto is a marked-up version of the changes made to the claims. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,

YOUNG & THOMPSON

By



Andrew J. Patch
Attorney for Applicants
Registration No. 32,925
745 South 23rd Street
Arlington, VA 22202
Telephone: 521-2297

April 4, 2002

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 8 has been amended as follows:

--8. (amended) The composition according to claim 7, wherein the organic creatine salt has a solubility above about 6 grams per 100 ml water.--

Claim 9 has been amended as follows:

--9. (amended) The composition according to claim 7, wherein the organic creatine salt further comprises an anionic component selected from the group of tartrate, maleate, malate, fumarate, citrate, and pyruvate.--

Claim 12 has been amended as follows:

--12. (amended) The composition according to claim [11] 9, wherein the anionic component of the creatine salt is a precursor of a Krebs cycle intermediate.--

Claim 14 has been amended as follows:

--14. (amended) The composition according to claim 1, comprising 1-10 gram creatine, [preferably provided by creatine citrate,] 0.6-5 gram phosphorus, [preferably provided by phosphate,] 0.1-15 gram buffer, [preferably a combination of carbonate and/or bicarbonate and citrate,] and 1-100 g of digestible carbohydrates.--

Claim 16 has been amended as follows:

--16. (amended) The composition according to claim 1, further comprising a pentose[, preferably ribose].--

STOUT et al. S.N. 09/769,245

Claim 17 has been amended as follows:

--17. (amended) The composition according to claim 1, further comprising a sodium salt[, preferably sodium phosphate].--